

Amendments to the Claims:

This listing of claims replaces all prior versions and listings of claims in the application:

Listing of Claims:

- 1-9. (Cancelled)
10. (Currently amended) A method, comprising:
  - (a) studying ~~the interaction of~~ whether one or more chemical or biochemical test species ~~with~~ binds a three-dimensional structure of ~~[[a]] an~~ RGS4 polypeptide including at least a core region of a free ~~an~~ RGS4 protein; and
  - (b) selecting a potential modulator of an RGS protein from the one or more chemical or biochemical test species based on ~~the interaction of~~ whether the one or more chemical or biochemical test species ~~with~~ binds the three-dimensional structure of the polypeptide.
11. (Currently amended) The method of claim 10, wherein the free RGS4 protein has a G $\alpha$  binding site, and the potential modulator is selected based on ~~its interaction with~~ whether it binds the G $\alpha$  binding site of the free RGS4 protein.
12. (Currently amended) The method of claim 10, wherein the free RGS4 protein has an allosteric binding site, and the potential modulator is selected based on ~~its predicted interaction with~~ whether it binds the allosteric binding site of the free RGS4 protein.
13. (Previously Presented) The method of claim 12, wherein the free RGS4 protein includes an  $\alpha_1$ - $\alpha_2$  region, and the allosteric binding site of the free RGS4 protein is located in the  $\alpha_1$ - $\alpha_2$  region of the free RGS4 protein.

14. (Currently amended) The method of claim 10, wherein the free RGS4 protein includes an  $\alpha_6$ - $\alpha_7$  region, and the potential modulator is selected based on ~~its predicted interaction with~~ whether it binds the  $\alpha_6$ - $\alpha_7$  region of the free RGS4 protein.

15. (Previously Presented) The method of claim 10, wherein the chemical or biochemical test species comprise small organic molecules.

16. (Previously Presented) The method of claim 10, further comprising:  
(c) obtaining the potential modulator; and  
(d) assaying the potential modulator to measure its activity as a modulator of RGS activity, RGS binding or RGS-G $\alpha$  complex activity.

17. (Cancelled).

18. (Currently amended) A process, comprising:  
identifying a substance that inhibits RGS4 activity, RGS4 binding or RGS4 G $\alpha$  complex activity by determining the interaction between whether a candidate species and binds a free RGS protein using a three-dimensional structure of [[a]] an RGS4 polypeptide including at least a core region of a free RGS4 protein.

19. (Cancelled).

20. (Currently amended) A method, comprising:  
(a) designing a potential modulator that will form a bond with one or more amino acids in the RGS4 G $\alpha$  binding site of a free RGS4 protein based upon a three-dimensional structure of [[a]] an RGS4 polypeptide including at least a core region of the free RGS4 protein;  
(b) synthesizing or otherwise obtaining the potential modulator; and

(c) determining whether the potential modulator inhibits or promotes the activity of RGS or RGS4/G $\alpha$  complex.

21. (Currently amended) The method of claim 20, wherein the RGS4 G $\alpha$  binding site includes one or more amino acids, the potential modulator is designed to ~~interact with~~ bind one or more atoms of the one or more amino acids in the RGS4 G $\alpha$  binding site, and the one or more amino acids are selected from the group consisting of D117, S118, and R121.

22. (Currently amended) The method of claim 20, wherein the RGS4 G $\alpha$  binding site includes one or more amino acids, the potential modulator is designed to ~~interact with~~ bind one or more atoms of the one or more amino acids in the RGS4 G $\alpha$  binding site, and the one or more amino acids are selected from the group consisting of S39, E41, N42, L113, D117, S118, R121, and N82.

23. (Currently amended) A method, comprising:

(a) designing a potential modulator that will form a bond with one or more amino acids in the allosteric binding site in the  $\alpha$ 1- $\alpha$ 2 region of a free RGS4 protein based upon a three-dimensional structure of [[a]] an RGS4 polypeptide including at least a core region of the free RGS4 protein;

(b) synthesizing or otherwise obtaining the potential modulator; and

(c) determining whether the potential modulator inhibits or promotes the activity of RGS or RGS4/G $\alpha$  complex.

24. (Currently amended) The method of claim 23, wherein the allosteric binding site includes one or more amino acids, the modulator is designed to ~~interact with~~ bind one or more atoms of the one or more amino acids in the allosteric binding site, and the one or more amino acids is selected from the group consisting of V10, W13, L17, 120, H23, E24, C25 and T132.

25. (Cancelled).

26. (Currently amended) A method of identifying modulators of RGS activity, RGS binding or RGS4/G $\alpha$  complex activity by rational drug design, the method comprising:

- (a) designing a potential modulator that will form a bond with one or more amino acids in the  $\alpha_6$ - $\alpha_7$  region of a free RGS4 protein based upon a three-dimensional structure of [[a]] an RGS4 polypeptide including at least a core region of the free RGS4 protein;
- (b) synthesizing or otherwise obtaining the potential modulator; and
- (c) determining whether the potential modulator inhibits or promotes the activity of RGS or RGS4-G $\alpha$  complex.

27. (Previously Presented) The method of claim 26, wherein an activity of the potential modulator is assessed using an enzyme assay.

28. (Currently amended) A method, comprising:

- (a) providing a three dimensional structure of [[a]] an RGS4 polypeptide including at least a core region of a free RGS4 protein;
- (b) employing the three dimensional structure of the RGS4 polypeptide to select a potential antagonist or agonist of an RGS protein; and
- (c) synthesizing or otherwise obtaining the potential antagonist or agonist.

29. (Previously Presented) The method of claim 28, wherein the free RGS4 is defined by the relative structural coordinates according to Table 2,  $\pm$  a root mean square deviation of not more than 1.5 Å from the conserved backbone atoms of the amino acids of the core region of the free RGS4 protein.

30-32. (Cancelled).

33. (Previously Presented) The method of claim 28, wherein step (b) comprises identifying a chemical or biochemical species that will bind to the free RGS4 protein.

34. (Previously Presented) The method of claim 33, wherein the free RGS4 protein includes a  $G\alpha$  binding site, and the chemical or biochemical species is a protein that binds to the  $G\alpha$  binding site of the free RGS4 protein.

35. (Previously Presented) The method of claim 33, wherein the free RGS4 protein includes an  $\alpha_1$ - $\alpha_2$  region with an allosteric binding site, and the chemical or biochemical species binds to the allosteric binding site in the  $\alpha_1$ - $\alpha_2$  region of the free RGS4 protein.

36. (Previously Presented) The method of claim 33, wherein the RGS4 protein includes an  $\alpha_6$ - $\alpha_7$  region, and the chemical or biochemical species binds to the  $\alpha_6$ - $\alpha_7$  region of the free RGS4 protein.

37. (Previously Presented) The method of claim 33, further comprising testing the potential antagonist or agonist as a modulator of RGS protein activity, RGS binding, or RGS- $G\alpha$  complex activity.

38-44. (Cancelled).

45. (Previously Presented) The method of claim 10, wherein the free RGS4 protein is from a mammalian species.

46. (Previously Presented) The method of claim 10, wherein the free RGS4 protein is from a human.

47. (Previously Presented) The method of claim 10, wherein the potential modulator is an agonist of the RGS protein.

48. (Previously Presented) The method of claim 10, wherein the potential modulator is an antagonist of the RGS protein.

49. (Previously Presented) The method of claim 10, wherein the core region of the free RGS4 is defined by the relative structural coordinates of Table 2,  $\pm$  a root mean square deviation of not more than 1.5 Å from the conserved backbone atoms of the amino acids of the core region of the free RGS4 protein.

50. (Previously Presented) The method of claim 20, wherein the free RGS4 protein is from a mammalian species.

51. (Previously Presented) The method of claim 20, wherein the free RGS4 protein is from a human.

52. (Previously Presented) The method of claim 20, wherein the potential modulator is an agonist of the RGS protein.

53. (Previously Presented) The method of claim 20, wherein the potential modulator is an antagonist of the RGS protein.

54. (Previously Presented) The method of claim 20, wherein the core region of the free RGS4 is defined by the relative structural coordinates of Table 2,  $\pm$  a root mean square deviation of not more than 1.5 Å from the conserved backbone atoms of the amino acids of the core region of the free RGS4 protein.

55. (Previously Presented) The method of claim 23, wherein the free RGS4 protein is from a mammalian species.

56. (Previously Presented) The method of claim 23, wherein the free RGS4 protein is from a human.

57. (Previously Presented) The method of claim 23, wherein the potential modulator is an agonist of the RGS protein.

58. (Previously Presented) The method of claim 23, wherein the potential modulator is an antagonist of the RGS protein.

59. (Previously Presented) The method of claim 23, wherein the core region of the free RGS4 is defined by the relative structural coordinates of Table 2,  $\pm$  a root mean square deviation of not more than 1.5 Å from the conserved backbone atoms of the amino acids of the core region of the free RGS4 protein.

60. (Previously Presented) The method of claim 26, wherein the free RGS4 protein is from a mammalian species.

61. (Previously Presented) The method of claim 26, wherein the free RGS4 protein is from a human.

62. (Previously Presented) The method of claim 26, wherein the potential modulator is an agonist of the RGS protein.

63. (Previously Presented) The method of claim 26, wherein the potential modulator is an antagonist of the RGS protein.

64. (Previously Presented) The method of claim 26, wherein the core region of the free RGS4 is defined by the relative structural coordinates of Table 2,  $\pm$  a root mean square deviation of not more than 1.5 Å from the conserved backbone atoms of the amino acids of the core region of the free RGS4 protein.

65. (Previously Presented) The method of claim 28, wherein the free RGS4 protein is from a mammalian species.

66. (Previously Presented) The method of claim 28, wherein the free RGS4 protein is from a human.